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| EXAMINER | |
|---|---|
| SZPERKA, MICHAEL EDWARD | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | |

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/651,674 | ROODMAN ET AL. | |
| | Examiner | Art Unit | |
| | Michael Szperka | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-28 is/are pending in the application.

4a) Of the above claim(s) 1-23 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 24-28 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 2/20/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The Art Unit location and the examiner of your application in the USPTO have changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Michael Szperka, Group Art Unit 1644.

### *Election/Restrictions*

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 2, 4-5, 8-9, 11-14 and 21-23 are drawn to a method of resisting osteoclast formation using an anti-ECF-L antibody or active fragment thereof, classified in class 424, subclass 133.1.

II. Claims 3, 8-9 and 13-14 are drawn to a method of resisting osteoclast formation using an antisense oligonucleotide, classified in class 514, subclass 44.

III. Claims 6, 8-9, 13-14 and 17 are drawn to methods of resisting osteoclast formation using OPG, classified in class 424, subclass 85.1.

IV. Claims 7-9, 13-14 and 18 are drawn to methods of resisting osteoclast formation using RANK-Fc, classified in class 424, subclass 85.1.

V. Claims 16 and 19-20 are drawn to a method of resisting osteoclast formation using an anti-RANKL polyclonal antibody, classified in class 424, subclass 130.1

VI. Claims 24-28 are drawn to an isolated anti-ECF-L antibody or fragment thereof, classified in class 424, subclass 133.3.

2. Claim 1 links the inventions in Groups I-IV. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 1. Claim 10 links the inventions in Groups I and V. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim, claim 10. Claim 15 links the inventions of Groups III-V. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim, claim 15. Upon the allowance of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn and any claims depending from or otherwise including all the limitations of the allowable linking claims will be entitled to examination in the instant application. Applicants are advised that if any such claims depending from or including all the limitations of the allowable linking claims is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the

provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claims 8-9 and 13-14 are generic to Groups I-IV. These claims will be examined limited to the groups elected.

The inventions are distinct, each from the other because of the following reasons:

3. The inventions of Groups I-V are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The inventions of Groups I-V are drawn to methods of resisting osteoclast formation using either an anti-ECF-L antibody (Group I), an antisense S-oligonucleotide (Group II), OPG (Group III), RANK-Fc (Group IV) or an anti-RANKL polyclonal antibody (Group V). In the instant case the different inventions are not disclosed as capable of use together and will have different modes of operation. An anti-ECF-L antibody will operate by binding to ECF-L. An antisense oligonucleotide will operate by binding a target nucleotide sequence. OPG and RANK-Fc will each bind to RANKL but will operate differently based on their different sequences and structures. An anti-RANKL polyclonal antibody will operate by binding to RANKL. Therefore, the inventions of Groups I-V are unrelated.

4. The inventions of Groups II-V and Group VI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). The inventions of Groups II-V are drawn to methods of resisting osteoclast formation using either an antisense S-oligonucleotide (Group II), OPG (Group III), RANK-Fc (Group IV) or an anti-RANKL polyclonal antibody (Group V). The invention of Group VI is drawn to an isolated anti-ECF-L antibody or fragment thereof. In the instant case the different inventions are not disclosed as capable of use together and will have different modes of operation. The methods of Groups II-V will operate to inhibit ECF-L expression (Group II), to compete with RANK for RANKL binding sites (Groups III and IV) or to bind antigenic sites of RANKL (Group V). The invention of Group VI is an anti-ECF-L antibody that will operate by binding ECF-L antigenic sites. Therefore, the inventions of Groups II-V and VI are unrelated.

5. The inventions of Groups I and VI are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). The invention of Group I is drawn to a method of resisting osteoclast formation using an anti-ECF-L antibody. The invention of Group VI is drawn to an isolated anti-ECF-L antibody or fragment thereof. In the instant case the inventions of Group I and Group VI are distinct because the

product as claimed could be used in a materially different process of using that product. The anti-ECF-L antibody that is the invention of Group I can be used in a materially different process of using that product; e.g., to assay cell specific protein expression, for example. Therefore, the inventions of Groups I and VI are distinct.

6. Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and would require divergent searches of literature databases placing an undue administrative burden on the examiner, restriction for examination purposes as indicated is proper.

7. During a telephone conversation with Debora Anderson on 6/21/04 a provisional election was made with traverse to prosecute the invention of Group VI, claims 24-28. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-23 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

8. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

10. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re

Brouwer and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

***Specification***

11. The disclosure is objected to because of the following informalities:

A) It appears that a formatting error has occurred that renders Greek symbols as boxes throughout the specification. For example, see lines 13, 16, and 17 of page 3.

B) The sentence that ends on line 18 of page 23 contains two periods.

C) For the sake of enhanced clarity, full citations of non-patent literature sources are usually made in parenthetical notation, such as (Owhashi M ... 2000 Identification of ... J Biol Chem 275:1279-1286).

Appropriate correction is required.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is

requested in correcting any errors of which applicant may become aware in the specification.

Applicant is also reminded that the current status of parent application U.S.S.N. 10/650,277 is abandoned. An appropriate amendment to the specification is required.

***Claim Rejections - 35 USC § 112***

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 24-28 are rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. The sequences that correspond to ECF-L are critical and essential to the practice of the invention, but they are not included in the claims, and are not enabled by the disclosure. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Applicant has provided database accession numbers for the sequences of ECF-L. Specifically these are the human GenBank sequences NM_004000, AB025008 and AB025009. A disclosure of a patent should be complete in and of itself, and as such these sequences should be made part of the specification and referenced with SEQ ID numbers.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Applicant is reminded that such an amendment must be in compliance with the Sequence Rules, encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821-1.825. Applicant is also reminded to amend the specification (including the Brief Description of Drawings) and claims as appropriate to reflect compliance with the Sequence Rules.

14. Claims 24-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of antibodies that bind a mouse ECF-L molecule and antibodies that bind the human GenBank sequences NM_004000, AB025008 and AB025009.

Applicant is not in possession of anti-ECF-L antibodies that generically bind any ECF-L from any organism.

Applicant has claimed a broad genus of antibodies that bind ECF-L molecules that can be found in any organism and that have an undefined structure and sequence. The species described by applicant to support this genus are an antibody that specifically binds mouse ECF-L and the sequences of the human molecules that can be bound by an anti-ECF-L antibody. These sequences indicated by Applicant as being ECF-L on page 26, lines 10-18 of the instant specification are only present by reference to external documents. The annotations to the GenBank accession numbers identify the molecules as *Homo sapiens* chitinase 3-like 2 (CHI3L2) and *Homo sapiens* TSA1902-(L/S), a novel member of the chitinase family, rather than as ECF-L. A sequence very similar to TSA1902 has been deposited by Boot et al. (J Biol Chem 11/20/2000 online, 2001 276:6770-6778 paper) as AF290004 and is identified as *Homo sapiens* acidic mammalian chitinase precursor (see entire document, particularly Figure 8). Similarly, a molecule 99% identical to the mouse ECF-L disclosed in Figure 2 of Owhashi et al. (J Biol Chem, 2000, 275:1279-1286) was cloned by Jin et al. (Genomics 54:316-322) and labeled as Ym1 (see entire document, particularly Figure 1). Given this confusing state of nomenclature regarding the identity of ECF-L, a person of skill in the art would not know what molecule or molecules are considered by applicant to be

ECF-L without identifying such molecules in the specification and claims by SEQ ID number.

No guidance appears to be given in the specification that identifies the particular structure or requisite epitopes that must be bound by an antibody specific for ECF-L to produce an antibody with the desired functional properties. Given the high degree of similarity between chitinase sequences and the confusing nomenclature of ECF-L molecules as discussed above, it is impossible to describe the structural characteristics of the genus of antibodies that specifically bind ECF-L. In light of this, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus of all antibodies that bind and inhibit ECF-L activity. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

### *Claim Rejections - 35 USC § 102*

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

16. Claims 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Owhashi et al. (J Biol Chem, 2000, 275:1279-1286, see entire document).

Owhashi et al. teach the isolation and characterization of a novel cytokine that has chemotactic properties for eosinophils (see entire document, particularly the abstract). As part of the characterization of this cytokine, a monoclonal antibody specific for ECF-L was generated (see particularly the section titled *Antisera* near the top of the right column of page 1280). This antibody was able to inhibit eosinophil chemotaxis when added to cultures that contained ECF-L (see particularly Figure 3, Figure 4, and the left column of page 1282). Owhashi et al. do not indicate that their antibody inhibits ECF-L induced osteoclast formation.

Applicant has not claimed or disclosed a specific epitope of ECF-L that must be recognized by an antibody to preclude osteoclast formation. Owhashi et al. teach a molecule that has the structure of an antibody and has the functional property of binding to mouse ECF-L. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). As such, the claimed properties or functions, in the instant case the functional property of inhibiting osteoclast formation, are presumed to be inherent in the structure of the prior

art antibody. See MPEP 2112.01 section I. Applicant is required to provide evidence that the antibody of Owhashi et al. lacks the functional property of inhibiting osteoclast formation to overcome a *prima facie* case anticipation by the prior art. See MPEP 2112 section V. Therefore, the prior art anticipates the claimed invention.

17. Claims 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakanishi et al., WO 01/36633, published on 5/25/01 (see entire document) as evidenced by Nakanishi et al., EP 1231270A1, published on 8/14/02 (see entire document).

EP1231270A1 is an English language national stage entry of PCT/JP00/08015 which was published in Japanese on 5/25/2001. As such, EP 123270A1 is an English language equivalent and is being used to provide evidence of the teachings contained in WO 01/36633 since an official translation is not currently available. See MPEP 2131.01. Please note that guidance to specific passages of the specification refer to the English language equivalent, EP 123270A1, and not WO 01/36633.

Nakanishi et al. teach the sequences of both murine and human ECF-L, and indicate that an antibody capable of inhibiting the activity of ECF-L would be useful in the treatment of diseases such as bronchial asthma and chronic obstructive pulmonary disease (see particularly the Abstract, Figure 8, paragraphs 231-237, 343-345, 349, and 354, and claim 13). The antibodies of the invention of Nakanishi et al. can be either monoclonal or polyclonal (see particularly paragraphs 146-157) and are suitable for administration to humans as a therapeutic or prophylactic agent (see particularly

paragraph 354). Nakanishi et al. do not indicate that their antibodies are capable of inhibiting ECF-L induced osteoclast formation. However, as was indicated above, since the antibodies of Nakanishi et al. specifically bind the same polypeptides as the claimed antibodies, and the antibodies of Nakanishi et al. have a therapeutic effect in a disease setting, the functional property of inhibiting osteoclast formation is an inherent property of the antibody in the absence of evidence to the contrary. See MPEP 2112.01. As such, the prior art anticipates the claimed invention.

18. Claims 24-28 are rejected under 35 U.S.C. 102(e) as being anticipated by Barash et al., US 2003/0152933A1 (see entire document).

Barash et al. disclose a sequence of 119 amino acids (SEQ ID NO:23) that is only one residue different from the C-terminus of the polypeptide encoded by GenBank accession number AB025008. This polypeptide has sequence homology to murine ECF-L, and an antibody directed against this sequence is useful in preventing chemoattractant activity and accumulation of leukocytes in situations such as adult respiratory distress syndrome (see particularly pages 6-7, the section titled Features of Protein Encoded by Gene No: 5, paragraphs 61 and 66, Table 1, and claim 13). It is disclosed that these antibodies can be monoclonal, human, humanized, or exist as fragments including Fab, Fab', $F(ab')_2$ and other engineered structures (see particularly the section titled Antibodies that spans pages 16-23, most particularly paragraphs 150

and 151). This disclosure is fully supported in their provisional application 60/225,215 filed on 8/14/2000.

Barash et al. do not disclose that their antibody has the functional property of inhibiting osteoclast formation. However, Applicant has not claimed or disclosed which amino acid residues must be recognized by an antibody in order to prevent ECF-L induced osteoclast formation. Without such information, the structure of the antibodies of Barash et al. and the claimed invention are identical. As such, the functional property of inhibiting osteoclast formation is an inherent property of the antibody directed to the polypeptide disclosed by Barash et al. in the absence of evidence to the contrary. See MPEP 2112.01. Therefore the prior art anticipates the claimed invention.

19. Claims 24-26 and 28 are rejected under 35 U.S.C. 102(e) as being anticipated by Elias et al., US2003/0049261A1 (see entire document).

Elias et al. teach compositions and methods for the treatment of inflammatory diseases including asthma, chronic obstructive pulmonary disease, inflammatory bowel disease, atopic dermatitis, atopy, allergy, allergic rhinitis, and scleroderma by inhibiting a chitinase-like molecule (see entire document, particularly the abstract). Chitinase-like molecules are particularly defined in paragraphs 15 and 78, and the use of an antibody as an inhibitor of a chitinase-like molecule is disclosed (see particularly paragraphs 16, 25, and 123, as well as claims 1-4). The molecules disclosed as being chitinase-like include NM_004000 and YM1 (also known as chitinase 3-like 3, ECF-L precursor, as

exemplified by GenBank accession number M94584). Data is also provided that indicates a therapeutic effect of antibodies to chitinase-like molecules in the treatment of a mouse asthma model (see particularly paragraph 252 and Figure 18), and that inhibiting Ym treats disease (see particularly paragraphs 109 and 113). The antibodies of Elias et al. are disclosed as being monoclonal, humanized and fragments (see particularly paragraph 99).

Elias et al. do not disclose that their antibody has the functional property of inhibiting osteoclast formation. However, the antibodies of Elias et al. have a structure that allows binding ECF-L molecules. This structure, in the absence of evidence to the contrary, is the same as Applicant's claimed invention and as such the functional property of inhibiting osteoclast formation is an inherent property of this structure. See MPEP 2112.01. Therefore the prior art anticipates the claimed invention.

### *Claim Rejections - 35 USC § 103*

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Nakanishi et al., WO 01/36633 (see entire document) or Nakanishi et al., EP 1231270A1 (see entire document), in view of Clark (Immunology Today, 2000, 21:397-402, see entire document).

The teachings of Nakanishi et al. have been discussed above. Even though Nakanishi et al. teach that their antibodies are suitable for therapeutic use *in vivo*, they differ from the claimed invention in that they do not indicate that the antibodies are human or humanized.

Clark taught that the antiglobulin response is a major problem in the clinical development of therapeutic antibodies (see entire document, particularly the abstract). This problem is exemplified by the human anti-murine-antibody (HAMA) response, in which a patient's immune system produces antibodies that neutralize the therapeutic antibodies administered to the patient, thus making repeated treatments with the therapeutic antibody ineffective (see particularly the paragraph that spans the left and right column of page 397). It is taught that humanization and fully human antibodies are strategies to avoid inducing a HAMA or an anti-therapeutic antibody response (see particularly the sections *Humanization to avoid the immune response* on page 399 and

*Alternative strategies for producing 'human' antibodies* on page 401). Elimination of this HAMA or anti-therapeutic antibody effect will allow for greater efficacy of therapeutic antibodies *in vivo* (see particularly the paragraph that spans pages 397 and 398).

It would have been obvious to a person of ordinary skill in the art at the time of the invention to produce human and humanized antibodies from the anti-ECF-L antibodies disclosed by Nakanishi et al. Motivation to do so comes from the greater utility of human or humanized antibodies for *in vivo* therapeutic use due to the diminished HAMA response as taught by Clark.

22. Claims 24-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elias et al., US2003/0049261A1 (see entire document) in view of Clark (Immunology Today, 2000, 21:397-402, see entire document).

The teachings of Elias et al. have been discussed previously. They differ from the claimed invention in that Elias et al. do not disclose that their therapeutic antibodies are human.

The teachings of Clark have been discussed previously.

A person of ordinary skill in the art at the time of the invention would have been motivated to make the therapeutic antibodies of Elias et al. human based on the advantage of the decreased HAMA response that is associated with the therapeutic use of such antibodies as taught by Clark. This decreased HAMA or anti-therapeutic antibody response allows for an improvement in the therapeutic efficacy of the antibody as taught by Clark.

23. No claims are allowable.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael Szperka, Ph.D.
Patent Examiner
Technology Center 1600
November 7, 2004

Patrick J. Nolan, Ph.D.
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